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NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS	4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS	5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS	6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS	7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS	8	NOV 20	CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS	9	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS	10	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS	11	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS	12	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS	13	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS	14	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS	15	DEC 18	CA/CAplus patent kind codes updated
NEWS	16	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS	17	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS	18	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS	19	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals

NEWS EXPRESS	NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
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NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

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=> file medline caplus embase biotechno biosis scisearch
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FILE 'SCISEARCH' ENTERED AT 08:56:07 ON 10 JAN 2007
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=> s irs-1
L1       12052 IRS-1

=> s l1 and antisense
L2         243 L1 AND ANTISENSE

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3           86 DUP REM L2 (157 DUPLICATES REMOVED)

=> d 1-86 ti

L3   ANSWER 1 OF 86  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Sorting nexins in the medical intervention of neurological and/or
     metabolic disorders

L3   ANSWER 2 OF 86  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Methods of modifying insulin signaling using biliverdin reductase, and
     treating conditions associated with insulin-mediated glucose uptake

L3   ANSWER 3 OF 86  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Genes showing changes in levels of expression in bladder cancer and their
     use in diagnosis and the development of antitumor agents

L3   ANSWER 4 OF 86  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Biomarkers for pre-selecting human cancer patients responsive to
     anti-IGF1R therapy

L3   ANSWER 5 OF 86  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Detection of human Frizzled proteins and application in treatment of
     cancer

L3   ANSWER 6 OF 86  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Methods for identifying regulators of G protein-coupled receptor kinase 2
     for treatment of type 2 diabetes mellitus

L3   ANSWER 7 OF 86  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Methods for identifying inhibitors of necdin promoting brown adipose
     tissue differentiation in treatment of obesity
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L3 ANSWER 8 OF 86 MEDLINE on STN DUPLICATE 1
TI Involvement of insulin-like growth factor type 1 receptor and protein kinase Cdelta in bis(maltolato)oxovanadium(IV)-induced phosphorylation of protein kinase B in HepG2 cells.

L3 ANSWER 9 OF 86 MEDLINE on STN DUPLICATE 2
TI Leptin inhibits apoptosis in thymus through a janus kinase-2-independent, insulin receptor substrate-1/phosphatidylinositol-3 kinase-dependent pathway.

L3 ANSWER 10 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Phosphoinositide-specific inositol polyphosphate 5-phosphatase IV inhibits inositide trisphosphate accumulation in hypothalamus and regulates food intake and body weight

L3 ANSWER 11 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Disruption of metabolic pathways - perspectives for the treatment of cancer

L3 ANSWER 12 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Diagnosis and treatment of pancreatic carcinoma by detecting and inhibiting aspartylpeptide β-di-oxygenase

L3 ANSWER 13 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Gene expression profiles in ovarian cancer and their use in diagnosis, prognosis, and selection of therapies

L3 ANSWER 14 OF 86 MEDLINE on STN DUPLICATE 3
TI Protein kinase C-alpha regulates insulin action and degradation by interacting with insulin receptor substrate-1 and 14-3-3 epsilon.

L3 ANSWER 15 OF 86 MEDLINE on STN DUPLICATE 4
TI Downregulation of IRS-1 expression causes inhibition of corneal angiogenesis.

L3 ANSWER 16 OF 86 MEDLINE on STN DUPLICATE 5
TI Up-regulation of insulin-like growth factor binding protein-3 by apigenin leads to growth inhibition and apoptosis of 22Rv1 xenograft in athymic nude mice.

L3 ANSWER 17 OF 86 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Up-regulation of insulin-like growth factor binding protein-3 by apigenin leads to growth inhibition and apoptosis of 22Rv1 xenograft in athymic nude mice

L3 ANSWER 18 OF 86 MEDLINE on STN DUPLICATE 6
TI Short-term in vivo inhibition of insulin receptor substrate-1 expression leads to insulin resistance, hyperinsulinemia, and increased adiposity.

L3 ANSWER 19 OF 86 MEDLINE on STN DUPLICATE 7
TI Involvement of endoplasmic reticulum stress in insulin resistance and diabetes.

L3 ANSWER 20 OF 86 MEDLINE on STN DUPLICATE 8
TI Suppressor of cytokine signaling-3 Provides a novel interface in the cross-talk between angiotensin II and insulin signaling systems.

L3 ANSWER 21 OF 86 MEDLINE on STN
TI PKCdelta and mTOR interact to regulate stress and IGF-I induced IRS-1 Ser312 phosphorylation in breast cancer cells.

L3 ANSWER 22 OF 86 MEDLINE on STN DUPLICATE 9

TI Melanin-concentrating hormone induces insulin resistance through a mechanism independent of body weight gain.

L3 ANSWER 23 OF 86 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Up-regulation of insulin-like growth factor binding protein-3 by apigenin leads to growth inhibition and apoptosis of 22Rv1 xenograft in athymic nude mice.

L3 ANSWER 24 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Method for increasing insulin sensitivity and for treating and preventing type 2 diabetes

L3 ANSWER 25 OF 86 MEDLINE on STN DUPLICATE 10
TI Suppressor of cytokine signaling 1 (SOCS-1) and SOCS-3 cause insulin resistance through inhibition of tyrosine phosphorylation of insulin receptor substrate proteins by discrete mechanisms.

L3 ANSWER 26 OF 86 MEDLINE on STN DUPLICATE 11
TI Inhibition of in vivo breast cancer growth by antisense oligodeoxynucleotides to type I insulin-like growth factor receptor mRNA involves inactivation of ErbBs, PI-3K/Akt and p42/p44 MAPK signaling pathways but not modulation of progesterone receptor activity.

L3 ANSWER 27 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Overexpression of ErbB2 receptor inhibits IGF-I-induced Shc-MAPK signaling pathway in breast cancer cells

L3 ANSWER 28 OF 86 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Cholinergic stimulus activates IRS-1/PI 3-kinase/Akt pathway in aorta of rats: A novel pathway to carbachol-induced eNOS activation.

L3 ANSWER 29 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Participation of prolactin receptors and phosphatidylinositol 3-kinase and MAP kinase pathways in the increase in pancreatic islet mass and sensitivity to glucose during pregnancy

L3 ANSWER 30 OF 86 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI PTPL1, a proapoptotic protein tyrosine phosphatase in breast cancers. Original Title: PTPL1, une proteine tyrosine phosphatase proapoptotique dans les cancers mammaires.

L3 ANSWER 31 OF 86 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Foot care behaviors after group classes.

L3 ANSWER 32 OF 86 MEDLINE on STN DUPLICATE 12
TI Screening for small molecule inhibitors of insulin-like growth factor receptor (IGF-1R) kinase: comparison of homogeneous time-resolved fluorescence and 33P-ATP plate assay formats.

L3 ANSWER 33 OF 86 MEDLINE on STN DUPLICATE 13
TI Restoration of insulin secretion in pancreatic islets of protein-deficient rats by reduced expression of insulin receptor substrate (IRS)-1 and IRS-2.

L3 ANSWER 34 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Insulin receptor signaling modulation-based methods and compositions for preventing obesity and obesity-related disorders

L3 ANSWER 35 OF 86 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on

STN
TI Development of new insulin-like growth factor-1 receptor kinase inhibitors using catechol mimics

L3 ANSWER 36 OF 86 MEDLINE on STN DUPLICATE 14
TI Cellular effects of small molecule PTP1B inhibitors on insulin signaling.

L3 ANSWER 37 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI SKIP negatively regulates insulin-induced GLUT4 translocation and membrane ruffle formation

L3 ANSWER 38 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Reversal of denervation-induced insulin resistance by SHIP2 protein synthesis blockade

L3 ANSWER 39 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Calpain facilitates GLUT4 vesicle translocation during insulin-stimulated glucose uptake in adipocytes

L3 ANSWER 40 OF 86 MEDLINE on STN DUPLICATE 15
TI Reduction of protein-tyrosine phosphatase-1B increases insulin signaling in FAO hepatoma cells.

L3 ANSWER 41 OF 86 MEDLINE on STN DUPLICATE 16
TI Reduction of protein tyrosine phosphatase 1B increases insulin-dependent signaling in ob/ob mice.

L3 ANSWER 42 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Antisense oligonucleotides for diagnosis and treatment of angiogenesis-related disorders by inhibition of genes encoding IRS -1 proteins

L3 ANSWER 43 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Compositions that inhibit proliferation of cancer cells

L3 ANSWER 44 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Proteins and nucleic acids associated with aging and their detection in identification of tissues undergoing senescence and of senescence modulators

L3 ANSWER 45 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Glucose regulates insulin mitogenic effect by modulating SHP-2 activation and localization in JAr cells

L3 ANSWER 46 OF 86 MEDLINE on STN DUPLICATE 17
TI RACK1, an insulin-like growth factor I (IGF-I) receptor-interacting protein, modulates IGF-I-dependent integrin signaling and promotes cell spreading and contact with extracellular matrix.

L3 ANSWER 47 OF 86 MEDLINE on STN DUPLICATE 18
TI Insulin receptor substrate-1 and phosphoinositide-dependent kinase-1 are required for insulin-stimulated production of nitric oxide in endothelial cells.

L3 ANSWER 48 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Blockade of IRS1 in isolated rat pancreatic islets improves glucose-induced insulin secretion

L3 ANSWER 49 OF 86 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Partial reversal of insulin secretion defect in pancreatic islets of protein deficient rats by antisense oligonucleotide blockade of IRS-1

L3 ANSWER 50 OF 86 MEDLINE on STN DUPLICATE 19
TI The type 2 vascular endothelial growth factor receptor recruits insulin receptor substrate-1 in its signalling pathway.

L3 ANSWER 51 OF 86 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Partial reversal of insulin secretion defect in pancreatic islets of protein deficient rats by antisense oligonucleotide blockade of IRS-1.

L3 ANSWER 52 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Diagnosis and treatment of malignant neoplasms by detecting and inhibiting aspartyl (asparaginyl) β-hydroxylase

L3 ANSWER 53 OF 86 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI G alpha(i2) enhances insulin signaling via suppression of protein-tyrosine phosphatase 1B

L3 ANSWER 54 OF 86 MEDLINE on STN DUPLICATE 20
TI Insulin receptor substrate-2 phosphorylation is necessary for protein kinase C zeta activation by insulin in L6hIR cells.

L3 ANSWER 55 OF 86 MEDLINE on STN
TI Regulation of breast cancer cell motility by insulin receptor substrate-2 (IRS-2) in metastatic variants of human breast cancer cell lines.

L3 ANSWER 56 OF 86 MEDLINE on STN DUPLICATE 21
TI Activation of the IGF-IR system contributes to malignant growth of human and mouse medulloblastomas.

L3 ANSWER 57 OF 86 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Pervanadate increases glucose uptake in MCF-7 breast cancer cells by a new undefined pathway that is insulin and insulin receptor substrate-1 (IRS-1) independent.

L3 ANSWER 58 OF 86 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Pervanadate increases insulin receptor (IR) phosphorylation and kinase activity through an increase in phosphorylated insulin receptor substrate-1 (IRS-1) in MCF-7 breast cancer cells.

L3 ANSWER 59 OF 86 MEDLINE on STN DUPLICATE 22
TI Characterization of the neurotrophic interaction between nerve growth factor and secreted alpha-amyloid precursor protein.

L3 ANSWER 60 OF 86 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 23
TI The receptor for the type I insulin-like growth factor and its ligands regulate multiple cellular functions that impact on metastasis.

L3 ANSWER 61 OF 86 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI The SUMO-conjugating enzyme Ubc9 is key for GLUT4 levels and insulin-stimulated glucose transport in 3T3-L1 adipocytes.

L3 ANSWER 62 OF 86 MEDLINE on STN DUPLICATE 24
TI Insulin-activated protein kinase Cbeta bypasses Ras and stimulates mitogen-activated protein kinase activity and cell proliferation in muscle cells.

L3 ANSWER 63 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Silibinin up-regulates insulin-like growth factor-binding protein 3

expression and inhibits proliferation of androgen-independent prostate cancer cells

L3 ANSWER 64 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Human rhabdomyosarcoma cells retain insulin-regulated glucose transport activity through glucose transporter 1

L3 ANSWER 65 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Identification of loci involved in accelerated wound healing and the development of new wound healing promoters

L3 ANSWER 66 OF 86 MEDLINE on STN DUPLICATE 25
TI In L6 skeletal muscle cells, glucose induces cytosolic translocation of protein kinase C-alpha and trans-activates the insulin receptor kinase.

L3 ANSWER 67 OF 86 MEDLINE on STN DUPLICATE 26
TI Inhibition of insulin-like growth factor I receptor signaling by the vitamin D analogue EB1089 in MCF-7 breast cancer cells: A role for insulin-like growth factor binding proteins.

L3 ANSWER 68 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Establishment of human rhabdomyosarcoma as an in vitro model for the study of insulin stimulated signal transduction and glucose transport

L3 ANSWER 69 OF 86 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Inhibition of tumorigenesis and induction of apoptosis in human tumor cells by the stable expression of a myristylated COOH terminus of the insulin-like growth factor I receptor

L3 ANSWER 70 OF 86 MEDLINE on STN DUPLICATE 27
TI Role of IRS-1 signaling in insulin-induced modulation of estrogen receptors in breast cancer cells.

L3 ANSWER 71 OF 86 MEDLINE on STN DUPLICATE 28
TI Insulin receptor substrate 1 antisense expression in an hepatoma cell line reduces cell proliferation and induces overexpression of the Src homology 2 domain and collagen protein (SHC).

L3 ANSWER 72 OF 86 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Insulin receptor substrate 1 antisense expression in an hepatoma cell line reduces cell proliferation and induces overexpression of the Src homology 2 domain and collagen protein (SHC).

L3 ANSWER 73 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Method and phosphopeptides for treatment of insulin resistance based on the association of protein tyrosine phosphatase 1B with the activated insulin receptor

L3 ANSWER 74 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Grb2-associated docking protein Gab1 in EGF- and insulin-receptor signaling

L3 ANSWER 75 OF 86 MEDLINE on STN DUPLICATE 29
TI Functional importance of Shc tyrosine 317 on insulin signaling in Rat1 fibroblasts expressing insulin receptors.

L3 ANSWER 76 OF 86 MEDLINE on STN
TI Requirement of protein kinase C zeta for stimulation of protein synthesis by insulin.

L3 ANSWER 77 OF 86 MEDLINE on STN DUPLICATE 30
TI Differential roles of IRS-1 and SHC signaling pathways

in breast cancer cells.

L3 ANSWER 78 OF 86 MEDLINE on STN DUPLICATE 31
TI Amyloid precursor protein requires the insulin signaling pathway for neurotrophic activity.

L3 ANSWER 79 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
TI Insulin action impaired by deficiency of the G-protein subunit Giα2

L3 ANSWER 80 OF 86 MEDLINE on STN DUPLICATE 32
TI The transmembrane protein-tyrosine phosphatase CD45 is associated with decreased insulin receptor signaling.

L3 ANSWER 81 OF 86 MEDLINE on STN DUPLICATE 33
TI The transmembrane protein-tyrosine phosphatase LAR modulates signaling by multiple receptor tyrosine kinases.

L3 ANSWER 82 OF 86 MEDLINE on STN DUPLICATE 34
TI Suppression of insulin receptor activation by overexpression of the protein-tyrosine phosphatase LAR in hepatoma cells.

L3 ANSWER 83 OF 86 MEDLINE on STN DUPLICATE 35
TI Overexpression of insulin receptor substrate 1 (IRS-1) in the human breast cancer cell line MCF-7 induces loss of estrogen requirements for growth and transformation.

L3 ANSWER 84 OF 86 MEDLINE on STN DUPLICATE 36
TI Transforming potential of the insulin receptor substrate 1.

L3 ANSWER 85 OF 86 MEDLINE on STN DUPLICATE 37
TI Insulin receptor substrate 1 mediates the stimulatory effect of insulin on GLUT4 translocation in transfected rat adipose cells.

L3 ANSWER 86 OF 86 MEDLINE on STN DUPLICATE 38
TI Functional expression of insulin receptor substrate-1 is required for insulin-stimulated mitogenic signaling.

=> d ab 15 28 42 51 70 71 77

L3 ANSWER 15 OF 86 MEDLINE on STN DUPLICATE 4
AB PURPOSE: The antiangiogenic effect of an antisense oligodeoxynucleotide (ODN) targeting insulin receptor substrate (IRS)-1 was evaluated on rat corneal neovascularization. METHODS: Eyes with neovessels were treated with subconjunctival injections of IRS-1 antisense oligonucleotide (ASODN), IRS-1 sense ODN (SODN), or PBS. At 8 and 24 hours after the first subconjunctival injection, the expression of IRS-1, VEGF, and IL-1beta mRNA was evaluated. IRS-1 protein levels were also measured at 8 hours by Western blot analysis (n = 4/group). On day 10, corneal neovascularization was quantified in flatmount corneas of rats treated daily from days 4 to 9. RESULTS: On day 10, new vessels covered 95.5% +/- 4% of the corneal area in PBS-treated eyes, 92% +/- 7% in SODN-treated eyes and 59% +/- 20% in ASODN-treated eyes ($P < 0.001$). In the ASODN-treated group, the expression and synthesis of IRS-1 were significantly downregulated when compared with the control groups. ASODN did not significantly affect the expression of VEGF but significantly decreased the expression of IL-1beta at 24 hours ($P = 0.04$). CONCLUSIONS: Subconjunctival injections of IRS-1 antisense ODN significantly inhibit rat corneal neovascularization. This effect may be mediated by a downregulation of IL-1beta. IRS-1 proteins may be interesting targets for the regulation of angiogenesis mediated by insulin, hypoxia, or inflammation.

L3 ANSWER 28 OF 86 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

L3 ANSWER 42 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
AB The invention relates to pharmaceutical compns. which inhibit the formation of capillary tubes by endothelial cells, comprising at least one oligonucleotide which can inhibit the expression of the IRS-1 (insulin receptor substrate 1) protein. According to the invention, the oligonucleotides are embodied as anti-angiogenesis agents. Said pharmaceutical compns. are particularly useful in treating angiogenesis-related pathologies.

L3 ANSWER 51 OF 86 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

L3 ANSWER 70 OF 86 MEDLINE on STN DUPLICATE 27
AB Cross-talk between steroid hormones and polypeptide growth factors regulates the growth of hormone-responsive breast cancer cells. For example, in the MCF-7 human breast cancer cell line, insulin up-regulates estrogen receptor (ER) content and binding capacity. Since the insulin receptor (IR) substrate 1 (IRS-1) is one of the core signaling elements transmitting mitogenic and metabolic effects of insulin, we investigated whether IRS-1 is also required for the insulin-induced function of the ER. The effects of insulin on the ER were compared in MCF-7 cells and MCF-7-derived cell lines with decreased levels (by approximately 80%) of IRS-1 due to the expression of IRS-1 antisense RNA. The severe IRS-1 deficiency in MCF-7 cells was associated with (1) reduced mitogenic response to 20 ng/ml insulin and 10% calf serum (CS), but not to 1 nM estradiol (E2); (2) loss of insulin-E2 synergism; (3) up-regulation of ER protein expression and binding capacity; and (4) loss of insulin-induced regulation of ER tyrosine phosphorylation. In conclusion, the data confirm the existence of the IR-ER cross-talk and suggest that IRS-1 -dependent signaling may contribute to the negative regulation of the ER expression and function in MCF-7 cells.
Copyright 1998 Academic Press.

L3 ANSWER 71 OF 86 MEDLINE on STN DUPLICATE 28
AB In mammalian cells, the insulin receptor substrate 1 protein (IRS -1) is a specific substrate for insulin and IGF-1 receptor tyrosine kinases which is involved in mediating metabolic and mitogenic actions of insulin and IGFs. In order to determine if IRS-1 is also essential in a chicken derived hepatoma cell line (LMH cells), IRS-1 gene has been invalidated in these cells. For this, we subcloned chicken IRS-1 gene in an antisense orientation into a mammalian expression vector driven by the cytomegalovirus early promoter. LMH cells were stably transfected with this construct or with the empty vector carrying only the neomycin resistance gene and selected for cIRS-1 expression. One subclone, C2, showed a complete repression of cIRS-1 expression at both protein and mRNA levels. Proliferation of C2 cells was dramatically reduced (54%) compared with Neo(r) cells. Furthermore this reduction was accompanied by a decrease in insulin-dependent [3H]thymidine incorporation, indicating a reduction in DNA synthesis. Insulin-dependent [U-14C]glucose incorporation into cellular lipids was also significantly reduced in C2 cell line suggesting an alteration in lipogenesis. In wild type LMH cells, SHC which is involved in Ras pathway, also served as a substrate for insulin receptor tyrosine kinase. In C2 cells, SHC expression, its association with the insulin receptor and its tyrosine phosphorylation were largely increased. Two forms of the regulatory subunit of PI 3-kinase were present: p85 and p55 forms. Furthermore, C2 cells displayed increased basal phosphatidylinositol (PI) 3'-kinase

activity. This report demonstrates a role for cIRS-1 in the metabolic and mitogenic actions of insulin in LMH cells. However, the overexpression of cIRS-1 antisense did not completely abolish cell proliferation. This may be explained by the exacerbation of an alternative pathway that only partly compensate for the knocking out of cIRS-1 gene: the overexpression of SHC.

L3 ANSWER 77 OF 86 MEDLINE on STN DUPLICATE 30
AB Several polypeptide growth factors stimulate breast cancer growth and may be involved in tumor progression. However, the relative importance of diverse growth factor signaling pathways in the development and maintenance of the neoplastic phenotype is largely unknown. The activation of such growth factor receptors as the insulin-like growth factor I receptor (IGF-I R), erbB-type receptors (erbB Rs) and FGF receptors (FGF Rs) controls the phenotype of a model breast cancer cell line MCF-7. To evaluate the function of 2 post-receptor signaling molecules, insulin receptor substrate-1 (IRS-1) (a major substrate of the IGF-IR) and SHC (a common substrate of tyrosine kinase receptors), we developed several MCF-7-derived cell clones in which the synthesis of either IRS-1 or SHC was blocked by antisense RNA. In MCF-7 cells, down-regulation of IRS-1 by 80-85% strongly suppressed anchorage-dependent and -independent growth and induced apoptotic cell death under growth factor- and estrogen-reduced conditions. The reduction of SHC levels by approximately 50% resulted in the inhibition of monolayer and anchorage-independent growth but did not decrease cell survival. Importantly, cell aggregation and the ability of cells to survive on the extracellular matrix were inhibited in MCF-7/anti-SHC clones, but not in MCF-7/anti-IRS-1 clones. Cell motility toward IGF was not attenuated in any of the tested cell lines, but motility toward EGF was decreased in MCF-7/anti-SHC clones. Our results suggest that in MCF-7 cells: 1) both IRS-1 and SHC are implicated in the control of monolayer and anchorage-independent growth; 2) IRS-1 is critical to support cell survival; 3) SHC is involved in EGF-dependent motility; and 4) normal levels of SHC, but not IRS-1, are necessary for the formation and maintenance of cell-cell interactions.

=> d 15 28 42 51 70 77

L3 ANSWER 15 OF 86 MEDLINE on STN DUPLICATE 4
AN 2005571664 MEDLINE
DN PubMed ID: 16249482
TI Downregulation of IRS-1 expression causes inhibition of corneal angiogenesis.
AU Andrieu-Soler Charlotte; Berdugo Marianne; Doat Marc; Courtois Yves; BenEzra David; Behar-Cohen Francine
CS Institut National de la Sante et de la Recherche Medicale (INSERM), Paris, France.
SO Investigative ophthalmology & visual science, (2005 Nov) Vol. 46, No. 11, pp. 4072-8.
Journal code: 7703701. ISSN: 0146-0404.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200512
ED Entered STN: 27 Oct 2005
Last Updated on STN: 22 Dec 2005
Entered Medline: 21 Dec 2005

L3 ANSWER 28 OF 86 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

AN 2006:155695 BIOSIS
DN PREV200600163519
TI Cholinergic stimulus activates IRS-1/PI 3-kinase/Akt pathway in aorta of rats: A novel pathway to carbachol-induced eNOS activation.
AU Zecchin, Henrique G. [Reprint Author]; Souza, Claudio T.; Carvalheira, Jose B.; Carneiro, Everado M.; Boschero, Antonio C.; Velloso, Lisio A.; Franchini, Kleber G.; Saad, Mario J.
SO Diabetes, (JUN 2004) Vol. 53, No. Suppl. 2, pp. A501.
Meeting Info.: 64th Annual Meeting of the American-Diabetes-Association. Orlando, FL, USA. June 04 -08, 2004. Amer Diabet Assoc.
CODEN: DIAEAZ. ISSN: 0012-1797.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 9 Mar 2006
Last Updated on STN: 9 Mar 2006

L3 ANSWER 42 OF 86 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:977994 CAPLUS
DN 138:49932
TI Antisense oligonucleotides for diagnosis and treatment of angiogenesis-related disorders by inhibition of genes encoding IRS -1 proteins
IN Al-Mahmood, Salman
PA Gene Signal, Iraq
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002103014	A2	20021227	WO 2002-FR2067	20020614
	WO 2002103014	A3	20040226		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	FR 2826010	A1	20021220	FR 2001-7805	20010614
	FR 2826010	B1	20050225		
	CA 2451874	A1	20021227	CA 2002-2451874	20020614
	EP 1409672	A2	20040421	EP 2002-751246	20020614
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	JP 2004538272	T	20041224	JP 2003-505336	20020614
	US 2004162257	A1	20040819	US 2003-735512	20031212
PRAI	FR 2001-7805	A	20010614		
	WO 2002-FR2067	W	20020614		

L3 ANSWER 51 OF 86 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2002:579784 BIOSIS
DN PREV200200579784
TI Partial reversal of insulin secretion defect in pancreatic islets of protein deficient rats by antisense oligonucleotide blockade of IRS-1.
AU Araujo, E. P. [Reprint author]; Amaral, M. E. C. [Reprint author];

Filiputti, E. [Reprint author]; Souza, C. T.; Boschero, A. C. [Reprint author]; Velloso, L. A.; Carneiro, E. M. [Reprint author]
CS Physiology and Biophysics, University of Campinas, Campinas, Brazil
SO Diabetologia, (August, 2002) Vol. 45, No. Supplement 2, pp. A 148. print.
Meeting Info.: 38th Annual Meeting of the European Association for the Study of Diabetes (EASD). Budapest, Hungary. September 01-05, 2002. European Association for the Study of Diabetes.
CODEN: DBTGAJ. ISSN: 0012-186X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 13 Nov 2002
Last Updated on STN: 13 Nov 2002

L3 ANSWER 70 OF 86 MEDLINE on STN DUPLICATE 27
AN 1999097234 MEDLINE
DN PubMed ID: 9878535
TI Role of IRS-1 signaling in insulin-induced modulation of estrogen receptors in breast cancer cells.
AU Ando S; Panno M L; Salerno M; Sisci D; Mauro L; Lanzino M; Surmacz E
CS Dipartimento di Biologia Cellulare, Universita' degli Studi della Calabria, Cosenza, Italy.. sando@diemme.it
NC DK48969 (NIDDK)
SO Biochemical and biophysical research communications, (1998 Dec 18) Vol. 253, No. 2, pp. 315-9.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199901
ED Entered STN: 2 Feb 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 20 Jan 1999

L3 ANSWER 77 OF 86 MEDLINE on STN DUPLICATE 30
AN 97456287 MEDLINE
DN PubMed ID: 9311601
TI Differential roles of IRS-1 and SHC signaling pathways in breast cancer cells.
AU Nolan M K; Jankowska L; Prisco M; Xu S; Guvakova M A; Surmacz E
CS Kimmel Cancer Institute, Thomas Jefferson University, Philadelphia, PA 19107, USA.
NC DK48969 (NIDDK)
SO International journal of cancer. Journal international du cancer, (1997 Sep 4) Vol. 72, No. 5, pp. 828-34.
Journal code: 0042124. ISSN: 0020-7136.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
ED Entered STN: 24 Dec 1997
Last Updated on STN: 3 Mar 2000
Entered Medline: 31 Oct 1997

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